

BRIEF COMMUNICATION

Service in Vietnam and Risk of Testicular Cancer

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A recent study of military working dogs serving during the period of the Vietnam conflict reported a significantly increased risk of testicular tumors and, independently, testicular dysfunction in dogs who served and died in Vietnam (1). Because carcinogenic risk to the dog can be a useful indicator of carcinogenic risk to humans (2-4), the possibility that Vietnam service led to an increased risk of testicular cancer in humans warrants investigation. To study this hypothesis, we abstracted information on military service from occupational histories generated in a previously reported case-control study of testicular cancer (5-8) and assessed the contribution of Vietnam service to testicular cancer risk.

Subjects and Methods

Selected for this study were case subjects aged 18-42 years, who had been newly diagnosed with testicular cancer between January 1, 1976, and June 30, 1981, and had been referred to one of three Washington, D.C., area hospitals (i.e., the National Naval Medical Center, the Walter Reed Army Medical Center, and the National Institutes of Health Clinical Center). Control subjects were male patients at the same hospital as the case subjects, but who

were newly diagnosed during the same period with cancers other than cancer of the genital tract. Cancer control subjects were chosen to avoid recall bias and bias due to differences in referral patterns (5-7). The control subjects were matched to the case subjects on age (± 2 years).

A standardized questionnaire was administered to each study participant by a trained interviewer. Information on military service was abstracted from occupational histories developed using the questionnaire (8). Response rates in the study were 88% for case subjects and 90% for control subjects, with successful interviews being obtained from 271 case subjects and 259 control subjects (7).

Because cryptorchidism and low birth weight (<5 lb) are both rare and strong risk factors for testicular cancer (5,6), all patients with either condition were eliminated from the present study. The analysis was further restricted to the 137 case subjects and 156 control subjects born prior to 1955. Because of the reported association between non-Hodgkin's lymphoma and Vietnam service (9), 26 non-Hodgkin's lymphoma patients were further excluded from the control group, resulting in 130 control subjects for the study.

Results

Vietnam service was associated with statistically significant, elevated testicular cancer risks of greater than twofold in the entire study group, among all veterans, or among only veterans who served during the Vietnam conflict (Table 1). Adjustment for smoking status and educational status had little effect on the odds ratios. Twenty-nine percent of Vietnam-era control subjects reported service in Vietnam in this study, consistent with published reports that 29%-33% of American military personnel serving during the Vietnam conflict were stationed in Southeast Asia (10). Although the odds ratios did not vary significantly with age at diagnosis, risk was greater for case subjects diagnosed before the age of 35; the odds ratios for Vietnam service were 2.6 for case subjects diagnosed before 30 years of age, 3.0 for

case subjects diagnosed from 30 to 34 years of age, and 1.1 for case subjects diagnosed after 35 years of age.

An analysis restricted to the 38 seminoma cases yielded an estimated odds ratio associated with Vietnam service among the entire study group of 1.8 (95% confidence interval = 0.6-5.1); $P = .30$. A similar analysis restricted to the 99 nonseminoma testicular cancer cases yielded an odds ratio estimate of 2.4 (95% confidence interval = 1.1-5.4); $P = .025$. Table 2, limited to military veterans, summarizes the effect of Vietnam service on testicular cancer risk by service branch. Risk was elevated in Vietnam veterans who served in the Army, Navy, and Air Force but not in those who served in the Marine Corps. The odds ratio for the Marine Corps did not, however, differ significantly from the odds ratios for the other service branches.

Discussion

The twofold increased risk of testicular cancer observed in Vietnam veterans in the current study is of the same magnitude as that observed in military working dogs who served in Vietnam (1). Risk was greater for younger Vietnam veterans, as was observed in the dog study (1). Examination of available information on job description, duty station, and dates of service for Vietnam veteran case subjects and control subjects provided no

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Table 1. Cases, controls, and odds ratio of testicular cancer associated with Vietnam service according to military service status of study subjects

Military service status	Vietnam service		Odds ratio (95% CI)*	P†
	Yes	No		
Veteran or civilian				
Cases	31	106	2.1 (1.0-4.4)	.03
Controls	17	113		
Veteran				
Cases	31	60	2.5 (1.1-5.7)	.02
Controls	17	62		
Vietnam-era veteran				
Cases	31	37	2.3 (1.0-5.5)	.04
Controls	17	42		

*Analysis stratified on age at diagnosis (<30 y, 30-34 y, >34 y); conditional maximum likelihood estimate with exact 95% confidence interval (CI).

†Two-sided exact *P* value.

Table 2. Proportion of Vietnam veterans among testicular cancer case subjects and control subjects according to branch of military service, with odds ratio for service in Vietnam

Service branch	Case	Control	Odds ratio (95% CI)*	P†
Army	19/44	9/31	2.8 (0.8-10.5)	.07
Navy	7/25	4/30	3.4 (0.6-23.8)	.14
Air Force	2/13	1/11	1.8 (0.1-117.8)	>.9
Marine Corps	3/9	3/7	0.7 (0.1-7.9)	>.9

*Analysis for Army and Navy stratified on age at diagnosis (see footnote for Table 1); conditional maximum likelihood estimate with exact 95% confidence interval (CI).

†Two-sided exact *P* value.

evidence implicating specific factors related to Vietnam service.

Many studies have examined cancer mortality rates in Vietnam veterans (11-17). One such study (11) reported a significant fivefold excess of testicular cancer deaths among Vietnam veterans, and another study (12) reported nonsignificantly elevated testicular cancer death rates among Vietnam veterans (proportional mortality ratios of 1.1 for Army and 1.3 for Marine Corps), while the remaining studies either have shown no effect of Vietnam service (13,14) or have not reported on testicular cancer (15-17). Because the rate of survival from testicular cancer is high, however, mortality studies may not be powerful or appropriate vehicles for examining this association.

Cancer incidence studies relevant to Vietnam service are fewer. The study of Air Force veterans of Operation Ranch Hand, the unit responsible for aerial spraying of herbicides in Vietnam, reported three testicular cancers among

995 Operation Ranch Hand veterans who sprayed the herbicide agent orange and no testicular tumors among 1299 Air Force veterans who were involved in air transport in Southeast Asia (18). A study of the incidence of cancer in male veterans who sought medical care from the U.S. Department of Veterans Affairs medical system during 1970-1982 reported no overall excess risk of testicular cancer in veterans compared with national cancer registry rates (19). Testicular cancer rates were elevated in veterans, however, from ages 20 to 32 years, and Vietnam veterans would be heavily represented in this age cohort.

Impaired spermatogenesis and the development of germ cell tumors may have common risk factors (20,21). The Vietnam Experience Study of the Centers for Disease Control noted diminished semen quality in Vietnam veterans 15+ years after duty in Vietnam (22). Decreases in sperm concentration have also been reported in selected Vietnam veterans from Texas

who were thought to have received high exposures to agent orange (23) and in a self-selected group of Vietnam veterans claiming similar exposure (24). Evaluation of the Operation Ranch Hand veterans, however, showed no difference in sperm quality compared with that in matched controls (25). Occupational exposure to 2,4-dichlorophenoxyacetic acid, a major component of agent orange, has recently been demonstrated to impair spermatogenesis, with persistent sperm abnormalities indicative of permanent damage to the germinal epithelium (26).

Although there is insufficient evidence at this time to conclude that service in Vietnam led to increased risk of testicular cancer or testicular dysfunction in men, further study is clearly warranted. More follow-up and more detailed analyses of the Operation Ranch Hand cohort may provide information on the possible etiologic role of agent orange in observed testicular abnormalities in Vietnam veterans. However, a study specifically designed to assess the impact of Vietnam service on testicular cancer risk would be required to evaluate other possible risk factors associated with Vietnam service.

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